STN Search History

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FILE 'HOME' ENTERED AT 12:06:08 ON 03 FEB 2003

=> file medline, caplus, biosis, embase, scisearch
L1          57 (PLASMODIUM OR MALARIA) AND (VACCIN## OR IMMUNO#######) AND
               (HEPATITIS (2A) CORE (A) PROTEIN OR HBC OR HBCAG)
L2          28 DUP REM L1 (29 DUPLICATES REMOVED)
L3        3312 (PLASMODIUM OR MALARIA) AND (VACCIN## OR IMMUNO#######) AND
               (CIRCUMSPOROZOITE)
L4        1419 L3 AND (B-CELL OR T-CELL OR (B (A) CELL) OR (T (A) CELL))
L5         328 L4 AND (B-CELL OR (B (A) CELL)) AND (T-CELL OR (T (A) CELL))
L6          152 DUP REM L5 (176 DUPLICATES REMOVED)
L7          119 L6 NOT PY>2000
8            0 L7 AND BIRKETT/AU
L9           0 L7 AND NARDIN/AU
L10          4 L7 AND (HEPATITIS (S) CORE)

=>  d his

     (FILE 'HOME' ENTERED AT 12:06:08 ON 03 FEB 2003)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH' ENTERED AT 12:08:08 ON
     03 FEB 2003
L1          57 S (PLASMODIUM OR MALARIA) AND (VACCIN## OR IMMUNO#######) AND (
L2          28 DUP REM L1 (29 DUPLICATES REMOVED)
L3        3312 S (PLASMODIUM OR MALARIA) AND (VACCIN## OR IMMUNO#######) AND (
L4        1419 S L3 AND (B-CELL OR T-CELL OR (B (A) CELL) OR (T (A) CELL))
L5         328 S L4 AND (B-CELL OR (B (A) CELL)) AND ( T-CELL OR (T (A) CELL)
L6          152 DUP REM L5 (176 DUPLICATES REMOVED)
L7          119 S L6 NOT PY>2000
L8            0 S L7 AND BIRKETT/AU
L9            0 S L7 AND NARDIN/AU
L10           4 S L7 AND (HEPATITIS (S) CORE)
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L10 ANSWER 1 OF 4 MEDLINE
TI **Hepatitis** B virus **core** and e antigen: immune recognition and use as a **vaccine** carrier moiety.
SO INTERVIROLOGY, (1996) 39 (1-2) 104-10.
Journal code: 0364265. ISSN: 0300-5526.
AU Schodel F; Peterson D; Milich D

L10 ANSWER 2 OF 4 MEDLINE
TI Hybrid **hepatitis** B virus **core** antigen as a **vaccine** carrier moiety: I. presentation of foreign epitopes.
SO JOURNAL OF BIOTECHNOLOGY, (1996 Jan 26) 44 (1-3) 91-6. Ref: 14
Journal code: 8411927. ISSN: 0168-1656.
AU Schodel F; Peterson D; Hughes J; Wirtz R; Milich D

L10 ANSWER 3 OF 4 MEDLINE
TI The hepatitis nucleocapsid as a **vaccine** carrier moiety.
SO ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, (1995 May 31) 754 187-201.
Journal code: 7506858. ISSN: 0077-8923.
AU Milich D R; Peterson D L; Zheng J; Hughes J L; Wirtz R; Schodel F

L10 ANSWER 4 OF 4 MEDLINE
TI Immunity to **malaria** elicited by hybrid **hepatitis** B virus **core** particles carrying **circumsporozoite** protein epitopes.
SO JOURNAL OF EXPERIMENTAL MEDICINE, (1994 Sep 1) 180 (3) 1037-46.
Journal code: 2985109R. ISSN: 0022-1007.
AU Schodel F; Wirtz R; Peterson D; Hughes J; Warren R; Sadoff J; Milich D

L2 ANSWER 1 OF 28 CAPLUS COPYRIGHT 2003 ACS
AN 2002:142851 CAPLUS
DN 136:215388
TI **Immunogenic** hepatitis B nucleocapsid protein (**HBc**) chimeric particles having enhanced stability
IN Birkett, Ashley J.
PA Apovia, Inc., USA
SO PCT Int. Appl., 290 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002014478	A2	20020221	WO 2001-US41759	20010816
	W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CO, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, MZ, NO, NZ, PL, RO, SG, SI, SK, TT, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2001085452	A5	20020225	AU 2001-85452	20010816
PRAI	US 2000-225843P	P	20000816		
	US 2000-226867P	P	20000822		
	US 2001-930915	A	20010815		
	WO 2001-US41759	W	20010816		

AB A chimeric, carboxy-terminal truncated hepatitis B virus nucleocapsid protein (core protein or **HBc**) is disclosed that is engineered for both enhanced stability of self-assembled particles and the display of an **immunogenic** epitope. The **immunogenic** epitope is a B cell epitope or T cell epitope derived from pathogen such as Streptococcus pneumonia, Cryptosporidium parvum, HIV, foot and mouth disease virus, influenza virus, Yersinia pestia, etc. The display of the **immunogenic** epitope is displayed in the **immunogenic** loop of **HBc**, whereas the enhanced stability of self-assembled particles is obtained by the presence of at least one heterologous cysteine residue near the carboxy-terminus of the chimer mol. Methods of making and using the chimers are also disclosed.

L2 ANSWER 2 OF 28 CAPLUS COPYRIGHT 2003 ACS
AN 2002:142465 CAPLUS
DN 136:198912
TI **Malaria vaccines** comprise **Plasmodium** CS protein and truncated hepatitis B virus nucleocapsid protein or **HBcAg**
IN Birkett, Ashley J.
PA Apovia, Inc., USA
SO PCT Int. Appl., 197 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002013765	A2	20020221	WO 2001-US25625	20010816
	W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CO, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, MZ, NO, NZ, PL, RO, SG, SI, SK, TT, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,				

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2001084967 A5 20020225 AU 2001-84967 20010816

PRAI US 2000-225813P P 20000816
US 2001-931325 A 20010815
WO 2001-US25625 W 20010816

AB A chimeric, carboxy-terminal truncated hepatitis B virus nucleocapsid protein (**HBc**) is disclosed that contains an **immunogen** for inducing the prodn. of antibodies to malarial proteins. An **immunogenic** malarial epitope is expressed between residues 78 and 79 of the **HBc immunogenic** loop sequence. The chimer preferably contains a **malaria**-specific T cell epitope and is preferably engineered for both enhanced stability of self-assembled particles and enhanced yield of those chimeric particles. Methods of making and using the chimers are also disclosed.

L2 ANSWER 3 OF 28 MEDLINE DUPLICATE 1

AN 2002678313 MEDLINE

DN 22326329 PubMed ID: 12438363

TI A modified hepatitis B virus core particle containing multiple epitopes of the **Plasmodium** falciparum circumsporozoite protein provides a highly **immunogenic malaria vaccine** in preclinical analyses in rodent and primate hosts.

AU Birkett A; Lyons K; Schmidt A; Boyd D; Oliveira G A; Siddique A; Nussenzweig R; Calvo-Calle J M; Nardin E

CS Apovia Inc., San Diego, California 92121, USA.

NC AI43830 (NIAID)

SO INFECTION AND IMMUNITY, (2002 Dec) 70 (12) 6860-70.
Journal code: 0246127. ISSN: 0019-9567.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 200301

ED Entered STN: 20021120
Last Updated on STN: 20030108
Entered Medline: 20030107

AB Despite extensive public health efforts, there are presently 200 to 400 million **malaria** infections and 1 to 2 million deaths each year due to the **Plasmodium** parasite. A prime target for **malaria vaccine** development is the circumsporozoite (CS) protein, which is expressed on the extracellular sporozoite and the intracellular hepatic stages of the parasite. Previous studies in rodent **malaria** models have shown that CS repeat B-cell epitopes expressed in a recombinant hepatitis B virus core (**HBc**) protein can elicit protective immunity. To design a **vaccine** for human use, a series of recombinant **HBc** proteins containing epitopes of **Plasmodium** falciparum CS protein were assayed for immunogenicity in mice [A. Birkett, B. Thornton, D. Milich, G. A. Oliveira, A. Siddique, R. Nussenzweig, J. M. Calvo-Calle, and E. H. Nardin, abstract from the 50th Annual Meeting of the American Society of Tropical Medicine and Hygiene 2001, Am. J. Trop. Med. Hyg. 65(Suppl. 3):258, 2001; D. R. Milich, J. Hughes, J. Jones, M. Sallberg, and T. R. Phillips, **Vaccine** 20:771-788, 2001]. The present paper summarizes preclinical analyses of the optimal P. falciparum **HBc vaccine** candidate, termed ICC-1132, which contains T- and B-cell epitopes from the repeat region and a universal T-cell epitope from the C terminus of the CS protein. The **vaccine** was highly **immunogenic** in mice and in Macaca fascicularis (cynomolgus) monkeys. When formulated in adjuvants suitable for human use, the **vaccine** elicited antisporozoite antibody titers that were logs higher than those obtained

in previous studies. Human **malaria**-specific CD4(+)-T-cell clones and T cells of ICC-1132-immunized mice specifically recognized **malaria** T-cell epitopes contained in the **vaccine**. In addition to inducing strong **malaria**-specific immune responses in naive hosts, ICC-1132 elicited potent anamnestic antibody responses in mice primed with P. falciparum sporozoites, suggesting potential efficacy in enhancing the sporozoite-primed immune responses of individuals living in areas where **malaria** is endemic.

L2 ANSWER 4 OF 28 SCISEARCH COPYRIGHT 2003 ISI (R)
AN 2001:321624 SCISEARCH
GA The Genuine Article (R) Number: 419JX
TI Serological, epidemiological, and molecular differences between human T-cell lymphotropic virus type 1 (HTLV-1)-Seropositive healthy carriers and persons with HTLV-I gag indeterminate western blot patterns from the Caribbean
AU Rouet F; Meertens L; Courouble G; Herrmann-Storck C; Pabingui R; Chancerel B; Abid A; Strobel M; Mauclere P; Gessain A (Reprint)
CS Inst Pasteur, Unite Oncol Virale, Dept Retrovirus, 28 Rue Dr Roux, F-75724 Paris 15, France (Reprint); Inst Pasteur, Unite Oncol Virale, Dept Retrovirus, F-75724 Paris 15, France; CHU Pointe A Pitre, Etablissment Francais Sang, Pointe A Pitre, Guadeloupe; CHU Pointe A Pitre, Biol Lab, Pointe A Pitre, Guadeloupe; CHU Pointe A Pitre, Serv Malad Infect & Dermatol, Pointe A Pitre, Guadeloupe
CYA France; Guadeloupe
SO JOURNAL OF CLINICAL MICROBIOLOGY, (APR 2001) Vol. 39, No. 4, pp. 1247-1253.
Publisher: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA.
ISSN: 0095-1137.
DT Article; Journal
LA English
REC Reference Count: 48
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB To investigate the significance of serological human T-cell lymphotropic virus type 1 (HLTV-1) Gag indeterminate Western blot (WB) patterns in the Caribbean, a 6-year (1993 to 1998) cross-sectional study was conducted with 37,724 blood donors from Guadeloupe (French West Indies), whose sera were routinely screened by enzyme **immunoassay** (EIA) for the presence of HTLV-1 and -2 antibodies. By using stringent WE criteria, 77 donors (0.20%) were confirmed HTLV-1 seropositive, whereas 150 (0.40%; $P < 0.001$) were considered HTLV seroindeterminate. Among them, 41.3% (62) exhibited a typical HTLV-1 Gag indeterminate profile (HGIP). Furthermore 76 (50.7%) out of the 150 HTLV-seroindeterminate subjects were sequentially retested, with a mean duration of follow-up of 18.3 months (range, 1 to 70 months). Of these, 55 (72.4%) were still EIA positive and maintained the same WE profile whereas the others became EIA negative. This follow-up survey included 33 persons with an HGIP. Twenty-three of them (69.7%) had profiles that did not evolve over time. Moreover, no case of HTLV-1 seroconversion could be documented over time by studying such sequential samples. HTLV-1 seroprevalence was characterized by an age-dependent curve, a uniform excess in females, a significant relation with hepatitis B core (**HBc**) antibodies, and a microcluster distribution along the Atlantic coast of Guadeloupe. In contrast, the persons with an HGIP were significantly younger, had a 1:1 sex ratio, did not present any association with **HBc** antibodies, and were not clustered along the Atlantic facade. These divergent epidemiological features, together with discordant serological screening test results for subjects with HGIP and with the lack of HTLV-1 proviral sequences detected by PCR in their peripheral blood mononuclear cell DNA, strongly suggest that an HGIP does not reflect true HTLV-1 infection. In regard to these

data, healthy blood donors with HGIP should be reassured that they are unlikely to be infected with HTLV-1 or HTLV-2.

L2 ANSWER 5 OF 28 MEDLINE DUPLICATE 2
AN 2001694047 MEDLINE
DN 21605988 PubMed ID: 11738741
TI Conversion of poorly **immunogenic malaria** repeat sequences into a highly **immunogenic vaccine** candidate.
AU Milich D R; Hughes J; Jones J; Sallberg M; Phillips T R
CS Vaccine Research Institute of San Diego (VRISD), 3030 Science Park Road, Suite 100, San Diego, CA 92121, USA.. dmilich@vrisd.org
NC R01 20720
R01 48730
SO VACCINE, (2001 Dec 12) 20 (5-6) 771-88.
Journal code: 8406899. ISSN: 0264-410X.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200204
ED Entered STN: 20011217
Last Updated on STN: 20020413
Entered Medline: 20020412
AB The recent success of a **Plasmodium** falciparum **malaria vaccine** consisting of circumsporozoite protein (CSP) T and B cell epitopes has rekindled interest in the development of a pre-erythrocytic **vaccine**. In order to optimize immunogenicity, well-characterized CSP-specific neutralizing B cell epitopes and a universal T cell epitope were combined with an efficient and flexible particulate carrier platform, the hepatitis B core antigen (**HBcAg**), to produce a novel pre-erythrocytic **vaccine** candidate. The **vaccine** candidate, V12.PF3.1, is a potent **immunogen** in mice eliciting unprecedented levels (greater than 10(6) titers) of sporozoite-binding antibodies after only two doses. The anti-sporozoite antibodies are long lasting, represent all IgG isotypes, and antibody production is not genetically restricted. CSP-specific CD4+ T cells are also primed by V12.PF3.1 immunization in a majority of murine strains. Furthermore, the hybrid **HBcAg**-CS particles can be produced inexpensively in bacterial expression systems. These and other characteristics suggest that V12.PF3.1 represents an efficient and economical P. falciparum **vaccine** candidate for use separately or in combination with other formulations.

L2 ANSWER 6 OF 28 MEDLINE
AN 2001667847 MEDLINE
DN 21570498 PubMed ID: 11713529
TI Haemoglobin C protects against clinical **Plasmodium** falciparum **malaria**.
AU Modiano D; Luoni G; Sirima B S; Simpore J; Verra F; Konate A; Rastrelli E; Olivieri A; Calissano C; Paganotti G M; D'Urbano L; Sanou I; Sawadogo A; Modiano G; Coluzzi M
CS Dipartimento di Scienze di Sanita Pubblica, Sezione di Parassitologia, WHO Collaborating Centre for Malaria Epidemiology and Control, University of Rome "La Sapienza", 00185, Rome, Italy.. david.modiano@uniroma1.it
SO NATURE, (2001 Nov 15) 414 (6861) 305-8.
Journal code: 0410462. ISSN: 0028-0836.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200112

ED Entered STN: 20011120
Last Updated on STN: 20020123
Entered Medline: 20011220

AB Haemoglobin C (**HbC**; beta6Glu --> Lys) is common in malarious areas of West Africa, especially in Burkina Faso. Conclusive evidence exists on the protective role against severe **malaria** of haemoglobin S (HbS; beta6Glu --> Val) heterozygosity, whereas conflicting results for the **HbC** trait have been reported and no epidemiological data exist on the possible role of the HbCC genotype. In vitro studies suggested that HbCC erythrocytes fail to support the growth of P. falciparum but **HbC** homozygotes with high P. falciparum parasitaemias have been observed. Here we show, in a large case-control study performed in Burkina Faso on 4,348 Mossi subjects, that **HbC** is associated with a 29% reduction in risk of clinical **malaria** in HbAC heterozygotes (P = 0.0008) and of 93% in HbCC homozygotes (P = 0.0011). These findings, together with the limited pathology of HbAC and HbCC compared to the severely disadvantaged HbSS and HbSC genotypes and the low betaS gene frequency in the geographic epicentre of betaC, support the hypothesis that, in the long term and in the absence of **malaria** control, **HbC** would replace HbS in central West Africa.

L2 ANSWER 7 OF 28 CAPLUS COPYRIGHT 2003 ACS
AN 2000:384227 CAPLUS
DN 133:29600
TI Capsid particles of hepatitis B core antigen for presentation of **immunogenic** components
IN Murray, Kenneth
PA Biogen, Inc., USA
SO PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000032625	A1	20000608	WO 1999-US28755	19991203
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	BR 9915942	A	20010821	BR 1999-15942	19991203
	EP 1135408	A1	20010926	EP 1999-961935	19991203
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002532387	T2	20021002	JP 2000-585266	19991203
	US 2002064533	A1	20020530	US 2001-873459	20010604
	NO 2001002760	A	20010806	NO 2001-2760	20010605
PRAI	US 1998-110911P	P	19981204		
	WO 1999-US28755	W	19991203		

AB The authors discloses the use of hepatitis B virus (HBV) core antigen particles for presentation to the immune system of multiple **immunogen** specificities. The **immunogens**, epitopes, or other related structures, are crosslinked or fused to HBV capsid-binding peptides that selectively bind to HBV core protein. Mixts. of different **immunogens** and/or capsid-binding peptide ligands may be

crosslinked to the same HBV core particle. Such resulting multicomponent or multivalent HBV core particles may be advantageously used in therapeutic and prophylactic **vaccines** and compns., as well as in diagnostic applications.

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 8 OF 28 CAPLUS COPYRIGHT 2003 ACS
AN 1999:736896 CAPLUS
DN 132:2786
TI Enhancing immune response to multiple CTL epitopes in fusion with a universal HTL epitopes and endoplasmic reticulum-translocating signal sequences from plasmid vector minigene and evaluating DNA **vaccines** in MHC class I transgenic mice
IN Fikes, John D.; Hermanson, Gary G.; Sette, Alessandro; Ishioka, Glenn Y.; Livingston, Brian; Chesnut, Robert W.
PA Epimmune, Inc., USA
SO PCT Int. Appl., 130 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9958658	A2	19991118	WO 1999-US10646	19990513
	WO 9958658	A3	20000420		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9940785	A1	19991129	AU 1999-40785	19990513
	EP 1078092	A2	20010228	EP 1999-924233	19990513
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2002520000	T2	20020709	JP 2000-548449	19990513
PRAI	US 1998-78904	A	19980513		
	US 1998-85751P	P	19980515		
	WO 1999-US10646	W	19990513		

AB A method of enhancing immune response to multiple CTL (cytotoxic T-cell) epitopes expressed from a plasmid vector by fusing them with a universal HTL (helper T-lymphocyte) epitope and reticulum-translocating signal sequences and evaluating DNA **vaccines** by using MHC class I transgenic mice was described. The prototype DNA **vaccine** (pMin.1)was derived from pcDNA3.1 and encoded nine dominant HLA-A2.1- and A11-restricted epitopes from the polymerase, envelope, and **core proteins** of **hepatitis** B virus and HIV. The coding sequences of PADRE (pan-DR epitope) universal Th cell epitope and an endoplasmic reticulum-translocating signal sequence (mouse **IG** .kappa. signal peptide) were fused with the coding sequence of the above nine CTL epitopes in the plasmid minigene to stimulate the immune response. Immunization of HLA transgenic mice with this construct resulted in: (1) simultaneous CTL induction against all nine CTL epitopes despite their varying MHC binding affinities; (2) CTL responses that were equiv. in magnitude to those induced against a lipopeptide known be **immunogenic** in humans; (3) induction of memory CTLs up to 4 mo after a single DNA injection; (4) higher epitope-specific CTL responses

than immunization with DNA encoding whole protein; and (5) a correlation between the immunogenicity of DNA-encoded epitopes in vivo and the in vitro responses of specific CTL lines against minigene DNA-transfected target cells. Examn. of potential variables in minigene construct design revealed that removal of the PADRE Th cell epitope or the signal sequence, and changing the position of selected epitopes, affected the magnitude and frequency of CTL responses. It was demonstrated that the simultaneous induction of broad CTL responses in vivo against multiple dominant HLA-restricted epitopes using a minigene DNA **vaccine** was feasible and the utility of HLA transgenic mice in development and optimization of **vaccine** constructs for human use is an attractive alternative approach.

L2 ANSWER 9 OF 28 MEDLINE DUPLICATE 3
AN 2000234699 MEDLINE
DN 20234699 PubMed ID: 10774666
TI The serological status of Solomon Island blood donors.
AU Lucas R E; Faoagali J L
CS Medical Unit, Honiara Central Hospital, Solomon Islands.. Rick.Lucas@nt.gov.au
SO SOUTHEAST ASIAN JOURNAL OF TROPICAL MEDICINE AND PUBLIC HEALTH, (1999 Sep) 30 (3) 542-5.
Journal code: 0266303. ISSN: 0125-1562.
CY Thailand
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; AIDS
EM 200006
ED Entered STN: 20000616
Last Updated on STN: 20000616
Entered Medline: 20000608
AB The serological status of Solomon Island blood donors in 1995 and in particular the seroprevalence of antibodies to Hepatitis B and C and prevalence of risk factors for these chronic infections was studied. A questionnaire of risk factors for Hepatitis B and C was undertaken. All blood donors had been previously screened for HIV antibody without any positive cases recorded. 598 donors had serum collected of which 36 samples (6.0%) were third generation HCV EIA antibody positive and 3 samples were RIBA positive but none were PCR positive. 25.1% of samples were positive for HBsAg and anti-**HBc** antibody was found in 84.4%. Elevated ALT levels (>35 U/l) were found in 6.5% of samples but there was no statistically significant association with HCV or HBsAg status. 15.4% were TPHA positive and 5.4% had RPR titers more than or equal to 1. Anti-HTLV-1 antibody was positive in 12.3% randomly selected samples. All 10 positive samples were then found to be antibody indeterminate with Western blot assay. Of the 585 samples with completed questionnaires, analysis of the relationship between anti-HCV status with tattoo status and ear piercing also failed to reach statistical significance. Consistent with other studies from tropical **malaria** -prone countries, a positive anti-HCV antibody test even by the third generation EIA is probably a false positive test in most cases. In addition, high prevalence rates of HBV, yaws or syphilis infection were demonstrated.

L2 ANSWER 10 OF 28 MEDLINE
AN 1998179732 MEDLINE
DN 98179732 PubMed ID: 9519208
TI Mannose binding protein deficiency is not associated with **malaria** , hepatitis B carriage nor tuberculosis in Africans.
AU Bellamy R; Ruwende C; McAdam K P; Thursz M; Sumiya M; Summerfield J; Gilbert S C; Corrah T; Kwiatkowski D; Whittle H C; Hill A V

CS Wellcome Trust Centre for Human Genetics, Oxford University, UK.
SO QJM, (1998 Jan) 91 (1) 13-8.
Journal code: 9438285. ISSN: 1460-2725.
Report No.: PIP-132116; POP-00274848.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Population; AIDS
EM 199804
ED Entered STN: 19980410
Last Updated on STN: 20021218
Entered Medline: 19980401
AB We retrospectively studied MBP genotypes in patients with **malaria**, tuberculosis (TB), and persistent hepatitis B virus (HBV) carriage, in clinics and hospitals in The Gambia. Children under 10 years with cerebral **malaria** and/or severe malarial anaemia, were compared with children with symptomatic, mild **malaria**, and controls of the same age and ethnicity. Adult TB cases with smear-positive pulmonary TB were compared with healthy blood donors from the same ethnic groups. **Malaria** cases and controls were tested for hepatitis B core antibody (anti-**HBc**) and surface antigen (HBsAg). TB patients were tested for HIV antibodies. Genotyping used sequence-specific oligonucleotide analysis to identify MBP variant alleles. Overall, 46% (944/2041) of patients and controls were homozygous for the wild-type MBP allele, 45% (922/2041) were carriers of a single variant allele and 8.6% (175/2041) had two variant alleles. Neither homozygotes nor heterozygotes for MBP variants were at increased risk of clinical **malaria**, persistent HBV carriage or TB. The most common mutation in Africans, the codon 57 variant allele, was weakly associated with resistance to TB (221/794 in TB cases and 276/844 in controls, p = 0.037). MBP deficiency is not a significant risk factor for persistent HBV, severe **malaria** nor pulmonary TB in West Africa.
Low serum mannose-binding protein (MBP), a calcium-dependent serum lectin that acts as an opsonin to promote phagocytosis, has been characterized as the most common immune deficiency. It has been suggested that MBP acts as a binding protein for mycobacteria and other intracellular pathogens, enabling them to enter host macrophages. The present study investigated the association between variant MBP alleles and **malaria**, tuberculosis, and hepatitis B virus (HBV) in adults and children in The Gambia. Of the 2041 Gambians screened for MBP mutations, 944 (46%) were homozygous for the wild-type allele, 922 (45%) were carriers of a single variant allele, and 175 (8.6%) possessed 2 mutant alleles. Compared to healthy controls, neither homozygotes nor heterozygotes for MBP genotypes were at increased risk of severe **malaria** (n = 504), HBV carriage (n = 337), or tuberculosis (n = 397). Stratification of patients by ethnic group did not alter this lack of relationship. However, the most common mutation in Africans--the codon 57 variant allele--was weakly associated with resistance to tuberculosis in both cases and controls. Although MBP deficiency may predispose to recurrent infections, this study failed to provide evidence that such a deficiency is a major risk factor for infectious diseases.

L2 ANSWER 11 OF 28 MEDLINE DUPLICATE 4
AN 1998020875 MEDLINE
DN 98020875 PubMed ID: 9382731
TI Immunization with hybrid hepatitis B virus core particles carrying circumsporozoite antigen epitopes protects mice against **Plasmodium** yoelii challenge.
AU Schodel F; Peterson D; Milich D R; Charoenvit Y; Sadoff J; Wirtz R
CS INSERM U 80, Pavillon P. Hopital Edouard Herriot, Lyon, France.
NC AI20720 (NIAID)

AI33562 (NIAID)
SO BEHRING INSTITUTE MITTEILUNGEN, (1997 Feb) (98) 114-9.
Journal code: 0367532. ISSN: 0301-0457.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199711
ED Entered STN: 19971224
Last Updated on STN: 19971224
Entered Medline: 19971110
AB The hepatitis B virus nucleocapsid antigen (**HBcAg**) was investigated as a carrier moiety for circumsporozoite protein (CS) repeat B cell epitopes of the rodent **malaria** agent **Plasmodium** yoelii. A vector expressing a hybrid gene coding for the dominant CS repeat epitope (QGPGAP)4 was constructed and transformed into avirulent Salmonella typhimurium. The resulting hybrid **HBcAg**-CS polyproteins were purified from recombinant Salmonella typhimurium. They purified as particles and displayed **HBc** as well as P. yoelii CS antigenicity. To investigate immunogenicity and protective efficacy, BALB/c mice were immunized with the hybrid **HBcAg**-CS particles. Immunization resulted in high titered antinative CS serum IgG antibody litres. BALB/c mice immunized with hybrid HBcAgCS particles were between 90-100% protected against subsequent P. yoelli challenge. Protective immunity persisted for a minimum of three months. These data confirm the previous suggestion (Schodel et al., 1994), that hybrid **HBcAg** particles could become a useful component of future human **malaria** **vaccines**.

L2 ANSWER 12 OF 28 MEDLINE DUPLICATE 5
AN 97116588 MEDLINE
DN 97116588 PubMed ID: 8957676
TI Hepatitis B virus core and e antigen: immune recognition and use as a **vaccine** carrier moiety.
AU Schodel F; Peterson D; Milich D
CS INSERM U 80, Hopital Edouard-Herriot, Lyon, France.
NC AI20720 (NIAID)
AI33562 (NIAID)
SO INTERVIROLOGY, (1996) 39 (1-2) 104-10.
Journal code: 0364265. ISSN: 0300-5526.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199703
ED Entered STN: 19970327
Last Updated on STN: 19970327
Entered Medline: 19970314
AB The hepatitis B virus (HBV) core gene codes for two partially colinear antigens: a secreted antigen (HBeAg) and the particulate core antigen (**HBcAg**), which assembles to form subviral particles and in virions contains the viral genome and polymerase. In this review we summarize data on the immune recognition of **HBc**/eA and recent progress in the use of **HBcAg** as a carrier moiety for heterologous epitopes. During HBV infection, **HBcAg** and HBeAg are important targets of antiviral immunity. **HBcAg** and HBeAg are serologically distinct but share all characterized T-cell epitopes. The particulate **HBcAg** can elicit T-cell-independent as well as T-cell-dependent antibody responses, HBeAg is a strictly T-cell-dependent antigen. Neonatal tolerance to maternally derived circulating HBeAg may facilitate chronic HBV infection after vertical transmission of HBV. In a murine transgenic

model, **HBc**/eAg-specific Th1 cells were more readily anergized, whereas Th2 cells more easily escaped tolerization. In human HBV infection, acute adult HBV infection with subsequent virus elimination was characterized by Th1-like alpha-HBV serum IgG subtype distribution, whereas a Th2-like distribution of IgG subtypes was observed during chronic infection. During chronic infection, core gene mutants which abolish HBeAg synthesis were frequently observed. To exploit the unusual immunogenicity of particulate **HBcAg** as a **vaccine** carrier moiety, insertion sites for foreign epitopes were defined in recombinant expression systems. While fusion of epitopes to the N-terminus required a linker sequence for surface accessibility, both fusion to the N-terminus and to the C-terminus was compatible with particle assembly and preserved the native antigenicity and immunogenicity of **HBcAg**. Epitope insertion at an immunodominant internal site of **HBcAg** reduced the **HBcAg** immunogenicity and antigenicity and most drastically enhanced the immunogenicity of the inserted foreign epitopes. This internal site of **HBcAg** was used to express circumsporozoite antigen (CS) repeat epitopes of two rodent **malaria** parasites and of **Plasmodium** falciparum. Purified hybrid **HBcAg**-CS proteins were particulate and displayed CS antigenicity as well as reduced native **HBc** antigenicity. Immunization of several mouse strains with **HBcAg**-CS hybrid particles resulted in high-titered serum anti-CS antibodies representing all murine IgG isotypes and protected BALB/c mice against plasmodial challenge. Immunization of mice with **HBcAg** or **HBcAg**-CS particles formulated on alum, complete Freund's or incomplete Freund's adjuvant resulted in equivalent anti-CS and anti-**HBc** serum antibody titers. Preexisting immunity to **HBcAg** did not significantly alter the immunogenicity of hybrid **HBcAg** particles suggesting that carrier-specific immune suppression does not limit the use of hybrid **HBcAg** with internal insertions. Immunization with **HBcAg**-CS particles universally primed **HBcAg**-specific T cells and in addition CS-specific T cells were if the insert contained a CS-specific T-cell site for the corresponding murine MHC class II haplotype. The internal amino acid position in **HBcAg** is therefore permissive for the inclusion of heterologous T-helper as well as B-cell epitopes.

L2 ANSWER 13 OF 28 MEDLINE DUPLICATE 6
AN 96351459 MEDLINE
DN 96351459 PubMed ID: 8717391
TI Hybrid hepatitis B virus core antigen as a **vaccine** carrier moiety: I. presentation of foreign epitopes.
AU Schodel F; Peterson D; Hughes J; Wirtz R; Milich D
CS INSERM U 80, Hopital Edouard Herriot, Lyon, France.
NC AI20720 (NIAID)
AI33562 (NIAID)
SO JOURNAL OF BIOTECHNOLOGY, (1996 Jan 26) 44 (1-3) 91-6. Ref: 14
Journal code: 8411927. ISSN: 0168-1656.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Biotechnology
EM 199610
ED Entered STN: 19961025
Last Updated on STN: 19961025
Entered Medline: 19961016
AB Hepatitis B virus (HBV) core antigen (**HBcAg**) is a highly **immunogenic** subviral particle. Here, we review recent progress in the use of **HBcAg** as a carrier moiety for heterologous epitopes.

To define surface exposed and **immunogenic** insertion sites for foreign epitopes in **HBcAg**, peptidic epitopes representing binding sites for virus neutralizing antibodies on the HBV surface antigens were inserted at different positions within **HBcAg** using genetic engineering in an Escherichia coli expression system (Schodel et al. (1992) J. Virol. 66, 106-114). While fusion to the N-terminus required a linker to become surface accessible, both fusion to the N-terminus and to the C-terminus was compatible with particle assembly and preserved the native antigenicity and immunogenicity of **HBcAg**. Fusion to an immunodominant internal site of **HBcAg** reduced the **HBcAg** immunogenicity and antigenicity and most drastically enhanced the immunogenicity of the inserted foreign epitope. This internal site of **HBcAg** was used to express circumsporozoite antigen (CS) repeat epitopes of two rodent **malaria** parasites and of **Plasmodium** falciparum (Schodel et al. (1994b) J. Exp. Med. 180, 1037-1046 and Schodel et al. (1995a) 95th ASM General Meeting, Washington DC, Abstr. E61). When purified from recombinant Salmonella typhimurium, the hybrid **HBcAg**-CS proteins were particulate and displayed CS antigenicity as well as reduced **HBc** antigenicity, as compared to native **HBcAg**. Immunization of several mouse strains with **HBcAg**-CS hybrid particles resulted in high titered serum anti-CS antibodies representing all murine IgG isotypes. Immunization of mice with **HBcAg** or **HBcAg**-CS particles formulated on alum, complete Freunds or incomplete Freunds adjuvant resulted in equivalent anti-CS and anti-**HBc** serum antibody titres. The possible influence of carrier-specific immunosuppression was examined and pre-existing immunity to **HBcAg** did not significantly alter the immunogenicity of hybrid **HBcAg** particles suggesting that they would be useful carrier moieties for repeated immunizations against multiple haptens or in immune subjects after HBV infection. Examination of T cell recognition of **HBcAg**-CS particles revealed that **HBcAg**-specific T cells were universally primed and CS-specific T cells were primed if the insert contained a CS-specific T cell recognition site. This indicates that the internal amino acid position in **HBcAg** is permissive for the inclusion of heterologous functional T helper as well as B cell epitopes. BALB/c mice immunized with **HBcAg**-CS1 were protected against P. berghei challenge to 90% and 100%, respectively, in two independent experiments.

L2 ANSWER 14 OF 28 MEDLINE DUPLICATE 7
AN 96342132 MEDLINE
DN 96342132 PubMed ID: 8718577
TI Hybrid hepatitis B virus core antigen as a **vaccine** carrier moiety. II. Expression in avirulent Salmonella spp. for mucosal immunization.
AU Schodel F; Kelly S; Tinge S; Hopkins S; Peterson D; Milich D; Curtiss R 3rd
CS INSERM U 80, Hopital Edouard Herriot, Lyon, France.
NC AI20720 (NIAID)
AI33562 (NIAID)
SO ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY, (1996) 397 15-21. Ref: 18
Journal code: 0121103. ISSN: 0065-2598.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199701
ED Entered STN: 19970219
Last Updated on STN: 20000407

Entered Medline: 19970123

AB Hepatitis B virus (HBV) core antigen (**HBcAg**) is a highly **immunogenic** subviral particle. We and others have defined insertion sites for heterologous epitopes and successfully used hybrid particles to generate B and T cell immunity (reviewed in: Schodel et al. 1994a, 1995). Here we shall review recent progress in constructing avirulent Salmonella spp. expressing hybrid **HBcAg** particles carrying different epitopes. Hybrid **HBcAg** particles carrying virus neutralizing epitopes of the hepatitis B virus pre-S region or repeat epitopes of plasmodial circumsporozoite antigens were previously described (Schodel et al. 1992, 1994b). Salmonella spp. can be attenuated by defined genetic means so that they become avirulent, yet preserve invasiveness after oral uptake. Hybrid **HBcAg**-pre-S particles were expressed in Salmonella typhimurium and S. typhi **vaccine** strains. A single oral immunization of mice with such live recombinant S. typhimurium strains elicited a high titered serum anti-pre-S1 IgG response. Similarly, circumsporozoite repeat epitopes of three different **malaria** parasites were expressed as **HBcAg**-CS hybrids in recombinant S. spp. and were found to be highly **immunogenic** after oral immunization. To analyze mucosal immune responses, BALB/c mice were immunized with recombinant phoPc S. typhimurium expressing **HBcAg** by various mucosal routes (Hopkins et al., 1995). All routes of immunization resulted in high titered serum and local antibodies against **HBcAg** and S. typhimurium LPS. However, nasal immunization was most efficient in generating pulmonary IgA and rectal immunization in eliciting rectal IgA, suggesting some compartmentalization of the mucosal immune response.

L2 ANSWER 15 OF 28 MEDLINE DUPLICATE 8
AN 95402991 MEDLINE
DN 95402991 PubMed ID: 7672831
TI Effectiveness of mandatory transmissible diseases screening in Indian blood donors.
AU Choudhury N; Ramesh V; Saraswat S; Naik S
CS Department of Transfusion Medicine, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow.
SO INDIAN JOURNAL OF MEDICAL RESEARCH, (1995 Jun) 101 229-32.
Journal code: 0374701. ISSN: 0971-5916.
Report No.: PIP-109982; POP-00249816.
CY India
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Population; AIDS
EM 199510
ED Entered STN: 19951026
Last Updated on STN: 20021101
Entered Medline: 19951019

AB This study was undertaken to determine the prevalence of transfusion transmitted diseases (TTDs) among local blood donors, the safety offered by the four mandatory tests (for HIV, HBsAg, syphilis and **malaria**) and to assess alanine aminotransferase (ALT) as a surrogate test. A total of 313 blood donors were tested for HBsAg, hepatitis B core (**HBc**) antibody, hepatitis C (HCV) antibody, HIV antibody, and IgM antibody to cytomegalovirus (CMV-IgM). The serum alanine aminotransferase levels were also done on each unit of blood. The prevalence of various markers was 7(2.2%) for HBsAg, 57 (18.2%) for anti **HBc** (total), 1 (0.3%) for anti HCV, 16 (5.1%) for anti CMV. None of the donors were positive for HIV, VDRL or **malaria**. ALT level was raised in 16.5 per cent of donors and showed no correlation with hepatitis markers. ALT was not found to be useful as a surrogate marker for routine screening of donors. Sensitive tests like ELISA and immunofluoresence for

malaria antigen should be applied for screening for **malaria**. VDRL test may be used to detect high risk donors rather than detection of syphilis when stored blood is used. HBsAg and HIV tests should be routinely done on every unit of blood and anti HCV tests should be done regularly, if possible.

L2 ANSWER 16 OF 28 MEDLINE DUPLICATE 9
AN 95351601 MEDLINE
DN 95351601 PubMed ID: 7542855
TI The hepatitis nucleocapsid as a **vaccine** carrier moiety.
AU Milich D R; Peterson D L; Zheng J; Hughes J L; Wirtz R; Schodel F
CS Department of Molecular Biology, Scripps Research Institute, La Jolla, California 92037, USA.
NC AI 20720 (NIAID)
AI 33562 (NIAID)
SO ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, (1995 May 31) 754 187-201.
Journal code: 7506858. ISSN: 0077-8923.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199508
ED Entered STN: 19950911
Last Updated on STN: 19970203
Entered Medline: 19950825
AB The "carrier effect," defined as the provision of T cell recognition sites physically linked to B cell epitopes in order to provide Th cell function for antibody synthesis, is well known. Peptides, proteins, and more recently particulate protein antigens have been used for this purpose. The hepatitis B core antigen represents a highly **immunogenic** antigen in humans as well as in experimental animal models. Studies in mice have provided insight into this enhanced immunogenicity. For example, **HBcAg** directly activates B cells (i.e., T cell independence), **HBcAg** elicits strong T cell responses, and **HBcAg** is efficiently processed and presented by antigen presenting cells (APCs). These characteristics suggested that **HBcAg** may be an ideal carrier moiety for B cell epitopes requiring additional Th cell function. Therefore, a number of HBV and non-HBV B cell epitopes have been chemically linked or fused by recombinant methods to **HBcAg** as a method to increase immunogenicity with significant success. We have designed bacterial expression vectors that allow insertion of heterologous B cell epitopes at various positions within **HBcAg** particles and permit efficient purification of hybrid **HBcAg** particles. Studies of positional effects have demonstrated that an internal insertion into a dominant **HBcAg**-specific B cell site represents a superior location for enhanced antibody production. Immunogenicity studies have been extended to protection against experimental challenge in several systems. For example, a **malaria** CS repeat sequence derived from P. berghei was inserted into **HBcAg** at the internal site, and purified hybrid **HBcAg**/CS particles were highly **immunogenic** and protected 100% of experimentally challenged BALB/c mice. This system has also been exploited for purposes of oral vaccination by expressing genes coding for hybrid **HBcAg** particles in live, avirulent **vaccine** strains of Salmonella species.

L2 ANSWER 17 OF 28 MEDLINE
AN 96051031 MEDLINE
DN 96051031 PubMed ID: 7495196
TI Immunoglobulin levels in **malaria** infected Nigerians with and without abnormal haemoglobin.
AU Odegbemi J O; Williams A I

CS Department of Chemical Pathology, College of Medicine, University of Ibadan.
SO AFRICAN JOURNAL OF MEDICINE AND MEDICAL SCIENCES, (1995 Mar) 24 (1) 21-5. Journal code: 7801013. ISSN: 0309-3913.
CY Nigeria
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199601
ED Entered STN: 19960217
Last Updated on STN: 19960217
Entered Medline: 19960111
AB Comparative studies were made between malarial parasitaemia in Nigerians with and without abnormal haemoglobins. The three main classes of immunoglobulins (i.e. IgG, A and M) were assayed in these groups of patients and the mean values were compared. Those with abnormal haemoglobins S or C (HbS or **HbC**) were compared with those with normal control haemoglobin A (HbA). HbSS malarial patients have the highest mean values of the 3 classes of immunoglobulins. This is followed by HbAS patients while patients with normal Hb have lowest mean values for IgG and IgM. The significance of the results is discussed.

L2 ANSWER 18 OF 28 CAPLUS COPYRIGHT 2003 ACS
AN 1995:319827 CAPLUS
DN 122:89367
TI Recombinant Salmonella strains containing antigens, their use in anti-malarial **vaccines**, and methods for their preparation
IN Curtiss, Roy, III; Schodel, Florian
PA Washington University, USA
SO PCT Int. Appl., 155 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9424291	A2	19941027	WO 1994-US4168	19940415
	WO 9424291	A3	19941208		
	W: AU, BB, BG, BR, BY, CA, CZ, FI, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, VN				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9467055	A1	19941108	AU 1994-67055	19940415
PRAI	US 1993-48166		19930415		
	WO 1994-US4168		19940415		

AB Live avirulent strains of Salmonella are constructed as **vaccines** and **immunogenic** compns. which contain at least one **immunogenic** antigenic determinant fused to the hepatitis B virus core antigen (**HbcAg**). When circumsporozoite protein repeats from **Plasmodium** falciparum or P. burghei are inserted between residues 1-75 and residues 81-156 of **HbcAg**, Salmonella strains expressing the recombinant protein can act as an antimalarial oral **vaccine**. Initially, avirulent strains of Salmonella typhi are constructed by the introduction of two or more deletion mutations affecting cAMP synthesis and utilization (.DELTA.cya .DELTA.crp .DELTA.cdt); the resulting strains are characterized for stability of phenotype, complete avirulence, and high immunogenicity. Oligonucleotides coding for the plasmodial amino acid repeat sequences, (NANP)4 from P. falciparum CS antigen and (DP4NPN)2 from P. berghei, are inserted between the **HbcAg** gene regions encoding amino acids 1-75 and 81-156. In addn., a fragment of the hepatitis B pre-S(2) sequence (amino acids

133-143) is preferably fused to the C-terminal end of the **HbcAg** /CS hybrid for use as a marker and to verify the expression of the hybrid protein. The recombinant expression vectors are inserted into avirulent Salmonella host cells by transformation. The Salmonella strains are also .DELTA.asd mutants, and the plasmid vectors encoding the plasmodial epitopes also encode aspartate .beta.-semialdehyde dehydrogenase, such that loss of Asd expression also causes loss of expression of the **Plasmodium** epitope-contg. polypeptides. Mice orally immunized with the avirulent Salmonella constructs were protected against P. berghei (malarial) challenge.

L2 ANSWER 19 OF 28 MEDLINE DUPLICATE 10
AN 94342820 MEDLINE
DN 94342820 PubMed ID: 7520465
TI Immunity to **malaria** elicited by hybrid hepatitis B virus core particles carrying circumsporozoite protein epitopes.
AU Schodel F; Wirtz R; Peterson D; Hughes J; Warren R; Sadoff J; Milich D
CS Department of Bacterial Diseases, Walter Reed Army Institute of Research, Washington, DC 20307-5100.
NC AI-20720 (NIAID)
AI-33562 (NIAID)
SO JOURNAL OF EXPERIMENTAL MEDICINE, (1994 Sep 1) 180 (3) 1037-46.
Journal code: 2985109R. ISSN: 0022-1007.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199409
ED Entered STN: 19941005
Last Updated on STN: 19960129
Entered Medline: 19940922
AB The hepatitis B virus (HBV) nucleocapsid antigen (**HBcAg**) was investigated as a carrier moiety for the immunodominant circumsporozoite (CS) protein repeat epitopes of **Plasmodium** falciparum and the rodent **malaria** agent P. berghei. For this purpose hybrid genes coding for [NANP]4 (C75CS2) or [DP4NPN]2 (C75CS1) as internal inserts in **HBcAg** (between amino acids 75 and 81) were constructed and expressed in recombinant Salmonella typhimurium. The resulting hybrid **HBcAg**-CS polypeptides purified from S. typhimurium were particulate and displayed CS and **HBc** antigenicity, however, the **HBc** antigenicity was reduced compared to native recombinant **HBcAg**. Immunization of several mouse strains with **HBcAg** -CS1 and **HBcAg**-CS2 particles resulted in high titer, P.berghei- or P.falciparum-specific anti-CS antibodies representing all murine immunoglobulin G isotypes. The possible influence of carrier-specific immunosuppression was examined, and preexisting immunity to **HBcAg** did not significantly affect the immunogenicity of the CS epitopes within **HBcAg**-CS1 particles. Similarly, the choice of adjuvant did not significantly alter the immunogenicity of **HBcAg**-CS hybrid particles. Immunization in complete or incomplete Freund's adjuvant or alum resulted in equivalent anti-**HBc** and anti-CS humoral responses. Examination of T cell recognition of **HBcAg**-CS particles revealed that **HBcAg**-specific T cells were universally primed and CS-specific T cells were primed if the insert contained a CS-specific T cell recognition site. This indicates that the internal site in **HBcAg** is permissive for the inclusion of heterologous pathogen-specific T as well as B cell epitopes. Most importantly, 90 and 100% of BALB/c mice immunized with **HBcAg**-CS1 particles were protected against a P. berghei challenge infection in two independent experiments. Therefore, hybrid **HBcAg**-CS particles may represent a useful approach for future **malaria vaccine**

development.

L2 ANSWER 20 OF 28 MEDLINE
AN 95046927 MEDLINE
DN 95046927 PubMed ID: 7958469
TI Development of recombinant Salmonellae expressing hybrid hepatitis B virus core particles as candidate oral **vaccines**.
AU Schodel F; Kelly S M; Peterson D; Milich D; Hughes J; Tinge S; Wirtz R; Curtiss R 3rd
CS Department of Bacterial Diseases, Walter Reed Army Institute of Research, Washington, DC.
NC AI20720 (NIAID)
AI33562 (NIAID)
SO DEVELOPMENTS IN BIOLOGICAL STANDARDIZATION, (1994) 82 151-8. Ref: 17
Journal code: 0427140. ISSN: 0301-5149.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199412
ED Entered STN: 19950110
Last Updated on STN: 19950110
Entered Medline: 19941221
AB This paper provides a review on the development of hepatitis core antigen as a **vaccine** carrier moiety and the use of recombinant Salmonella **vaccine** strains expressing hybrid **HBcAg** particles as live oral **vaccines**. Salmonella spp. can be attenuated by defined genetic means so that they become avirulent, yet preserve invasiveness after oral uptake. Oral immunization of mice with such avirulent candidate Salmonella typhimurium **vaccine** strains elicited serum antibody responses against a limited number of bacterial antigens. A highly **immunogenic** viral nucleocapsid antigen, hepatitis B virus core antigen (**HBcAg**) that can be expressed in prokaryotes was used as a carrier moiety for B-cell epitopes. Insertion sites with an enhanced immunogenicity for the carried epitopes were defined using HBV envelope protein virus neutralizing epitopes. An internal insertion site in **HBcAg** was found that drastically enhanced the immunogenicity of the foreign (pre-S1) epitope while reducing the immunogenicity of the carrier protein. Internally fused **HBc** /pre-S hybrid particles were expressed in Salmonella typhimurium and S. typhi **vaccine** strains. A single oral immunization of mice with such live recombinant S. typhimurium strains elicited a high titred serum anti-pre-S1 IgG response. Similarly, circumsporozoite repeat epitopes of three different **malaria** parasites were expressed as **HBcAg**/CS hybrids in recombinant S. spp. and were found to be highly **immunogenic**.

L2 ANSWER 21 OF 28 MEDLINE DUPLICATE 11
AN 94071525 MEDLINE
DN 94071525 PubMed ID: 8250629
TI **Plasmodium** falciparum sporozoite and entomological inoculation rates at the Ahero rice irrigation scheme and the Miwani sugar-belt in western Kenya.
AU Githeko A K; Service M W; Mbogo C M; Atieli F K; Juma F O
CS Kenya Medical Research Institute (KEMRI), Vector Biology and Control Research Centre, Kisumu.
SO ANNALS OF TROPICAL MEDICINE AND PARASITOLOGY, (1993 Aug) 87 (4) 379-91.
Journal code: 2985178R. ISSN: 0003-4983.
CY ENGLAND: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199401
ED Entered STN: 19940201
Last Updated on STN: 19940201
Entered Medline: 19940103
AB Anopheles arabiensis and An. funestus were collected by pyrethrum spray sheet collections in houses and by human-bait catches at a village in western Kenya adjacent to the Ahero rice irrigation scheme; and using the same methods, An. gambiae s.l. and An. funestus were collected at Miwani, a village in the sugar-cane belt. **Plasmodium** falciparum sporozoite rates were determined by ELISA. At Ahero the mean sporozoite rates were 1.1% and 4.3% in An. arabiensis and An. funestus, respectively, while at Miwani the rates were 6.0% in An. gambiae s.l. and 4.3% in An. funestus. Entomolgoical inoculation rates (EIR) were derived from both human-bait collections (IR-**HBC**) and by the proportion of human blood-fed females caught resting indoors (IR-HBF). The IR-HBF appeared to be a more realistic index of EIR. At Ahero and Miwani people were exposed to an average of 416 and 91 infective bites/person/year, respectively. The main vectors were An. funestus at Ahero and An. gambiae s.l. at Miwani. In view of the intense and perennial **malaria** transmission at Ahero, vector control by insecticides should be considered, while at Miwani, where transmission is seasonal, permethrin-impregnated bed nets could be an alternative to indoor spraying. These measures must be augmented with availability of effective antimalarials.

L2 ANSWER 22 OF 28 MEDLINE
AN 95278134 MEDLINE
DN 95278134 PubMed ID: 7758379
TI [Viral markers of acute hepatitis: A, B, C, D, and E in Dakar. October 92 - October 93].
Marqueurs viraux des hepatites aigues: A, B, C, D et E a Dakar. Octobre 92-Octobre 93.
AU Crato M; Michel P; Rodier G R; Ka M; Hugard L; Diouf G
CS Laboratoire de Virologie Medicale-Institut Pasteur, Dakar.
SO DAKAR MEDICAL, (1993) 38 (2) 183-5.
Journal code: 7907630. ISSN: 0049-1101.
CY Senegal
DT Journal; Article; (JOURNAL ARTICLE)
LA French
FS Priority Journals
EM 199506
ED Entered STN: 19950707
Last Updated on STN: 19980206
Entered Medline: 19950629
AB Inside of 95 patients presented in Hospital with presumed hepatitis: 77 were recruted with liver cytolysis (Amino-Transferases AT > 80 UI/ml) and included in this study. Study of serologic viral markers (A, B, C, D and E type) permited to prove viral acute hepatitis infection and 49 patients were recruted inside the 77 cytolytic cases. Inside these 49 cases: 44% presented enteritic contamination with HAV/HEV markers, 36% with HBV markers: HBs/**HBc**, 6% with HBs/HBe markers, 10% with HDV marker, 4% with HCV marker. 28 patients presented any viral acute hepatitis marker and in this case can be evocated other hepatitis origin: viral hepatitis type (EBV), CMV, chronic hepatitis evolution, **malaria** hepatitis or toxic hepatitis.

L2 ANSWER 23 OF 28 CAPLUS COPYRIGHT 2003 ACS
AN 1992:212835 CAPLUS
DN 116:212835

TI T-cell-stimulating peptide of hepatitis B core antigen (**HBcAg**)
IN Ferrari, Carlo; Colucci, Giuseppe
PA CLONIT S.p.A., Italy
SO Eur. Pat. Appl., 14 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 469281	A1	19920205	EP 1991-110233	19910621
	EP 469281	B1	19930616		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	AT 90689	E	19930715	AT 1991-110233	19910621
	ES 2058992	T3	19941101	ES 1991-110233	19910621
	CA 2048029	AA	19920201	CA 1991-2048029	19910729
	JP 05213995	A2	19930824	JP 1991-279035	19910730
	JP 3000569	B2	20000117		
PRAI	GB 1990-16727	A	19900731		
	EP 1991-110233	A	19910621		

AB A T-cell-stimulating peptide comprises PHHTALRQAILCWGELMTLA (I) (amino acid residues 50-69 of **HBcAg**). I may be linked to an **immunogen**. A **vaccine** comprising I or I linked to an **immunogen** is also claimed.

L2 ANSWER 24 OF 28 MEDLINE
AN 93332505 MEDLINE
DN 93332505 PubMed ID: 1307202
TI [Prevalence of antibodies to hepatitis C (anti HCV) in blood donors in Rio de Janeiro, Brazil. Its relation to ALT and anti **HBC**].
Prevalencia do anticorpo contra hepatite C (anti VHC) em doadores de sangue no Rio de Janeiro, Brasil. Sua relacao com ALT e anti **HBC**
.
CM Comment in: Arq Gastroenterol. 1992 Jan-Mar;29(1):1-4
AU Leite N C; Nogueira C M; Coelho H S; Perez R; Martins S J; Soares J A; Junqueira P C
CS Servico de Clinica, Hospital Universitario Clementino Fraga Filho, Universidade Federal do Rio de Janeiro.
SO ARQUIVOS DE GASTROENTEROLOGIA, (1992 Jan-Mar) 29 (1) 5-11.
Journal code: 15310600R. ISSN: 0004-2803.
CY Brazil
DT Journal; Article; (JOURNAL ARTICLE)
LA Portuguese
FS Priority Journals
EM 199308
ED Entered STN: 19930903
Last Updated on STN: 19980206
Entered Medline: 19930824
AB We have studied 933 volunteer blood donors from May to July, 1990. After a interview and screening tests for syphilis, Chagas disease, **malaria** and HIV, they underwent an enzyme **immunoassay** for HBsAg, anti **HBc** and anti HCV antibodies. Alanine aminotransferase (ALT) serum levels were determined by auto analyser. Most blood donors were male with mean age of 33 years (19-65). Anti HCV prevalence was 3.1% (29 from 933 blood donors). Among anti HCV+, blood donors, 44.8% (13/29) had ALT 40 UI/L, 31% (9/29) were anti **HBc**+ and 17.2% (5/29) had both surrogate markers simultaneously. From 109 donors with ALT 40 UI/L, 13 (11.9%) were anti HCV+, while among 153 anti **HBc**+ donors, the anti HCV was 5.8%. Conclusions: 1) we found a higher anti HCV prevalence among our blood donors than previous published reports from other countries; 2) our data show that surrogate assays do

not adequately identify anti HCV blood donors, 41.4% of them would not have been excluded by anti **HBc** and ALT tests alone; 3) there were a correlation between anti HCV positivity with a sample to cutoff optical density ratio equal or greater than 4 and elevated ALT serum levels.

L2 ANSWER 25 OF 28 MEDLINE
AN 91077461 MEDLINE
DN 91077461 PubMed ID: 2257317
TI Innate resistance to **malaria**: the intraerythrocytic cycle.
AU Nagel R L
CS Division of Hematology, Albert Einstein College of Medicine, Bronx, NY 10461.
SO BLOOD CELLS, (1990) 16 (2-3) 321-39; discussion 340-9. Ref: 90
Journal code: 7513567. ISSN: 0340-4684.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 199101
ED Entered STN: 19910322
Last Updated on STN: 19910322
Entered Medline: 19910131
AB The human innate resistance to P. falciparum **malaria** is based on genetic features that affect several stages of the intraerythrocytic cycle of the **plasmodia**. HbS, HbE and alpha and beta thalassemia (in addition to G-6PD deficiency) are protective to the carriers, because they inhibit the intraerythrocytic growth period, and in the case of AS red cells, in addition, parasitosis make them detectable expeditiously by the spleen. Blood group polymorphisms can interfere with red cell invasion by **plasmodia**. **HbC** belongs to a special category, since it apparently interferes with the cycle at the moment of cell lysis and release of merozoites. Finally, ovalocytosis observed in South East Asia, which most likely corresponds to a cytoskeleton or membrane protein defect, protects from **malaria** by inhibiting invasion. It should be kept in mind that many of these red cell defects might protect individuals in the critical first 5 years of life by retarding the switch of HbF to adult hemoglobin, since the HbF containing red cells are less than hospitable to the parasite.

L2 ANSWER 26 OF 28 MEDLINE
AN 89317049 MEDLINE
DN 89317049 PubMed ID: 2501850
TI [Transmissible diseases through the intermediary of transfusions]. Maladies transmissibles par l'intermediaire des transfusions.
AU Van Laethem Y
SO REVUE MEDICALE DE BRUXELLES, (1989 Apr) 10 (4) 125-30.
Journal code: 8003474. ISSN: 0035-3639.
CY Belgium
DT Journal; Article; (JOURNAL ARTICLE)
LA French
FS Priority Journals; AIDS
EM 198908
ED Entered STN: 19900309
Last Updated on STN: 19900309
Entered Medline: 19890825
AB Blood transfusions may lead to **immunologic** but also infectious problems. If bacterial pathogens are rarely involved, blood pathogens - especially **malaria** - and viruses are dominant. Non-a non-b

hepatitis is the most frequently encountered viral infection, with a risk of 1% for each blood unit. Screening of SGPT and anti **Hbc** antibodies should diminish the transmission risk by 30-40%. Since August 1985, HIV antibody screening of blood donors has dramatically reduced the risk of blood transmission; however, patients Ag HIV+/Ac HIV (first weeks of infection, ...) imply that severe voluntary exclusion procedures are maintained for the donors; similar measures are also valid for **malaria** prevention.

L2 ANSWER 27 OF 28 CAPLUS COPYRIGHT 2003 ACS
AN 1990:113595 CAPLUS
DN 112:113595
TI Fusion proteins composed of hepatitis B core antigen (**HBcAg**) and noncorresponding epitope, and their recombinant preparation
PA Wellcome Foundation Ltd., USA
SO Jpn. Kokai Tokkyo Koho, 11 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 63196299	A2	19880815	JP 1987-52829	19870307
	AU 8769792	A1	19880811	AU 1987-69792	19870306
	AU 596154	B2	19900426		
	CA 1319628	A1	19930629	CA 1987-534146	19870408
	AU 9049273	A1	19900809	AU 1990-49273	19900208
	AU 642859	B2	19931104		
PRAI	US 1987-12948		19870210		

AB A fusion protein comprising a noncorresponding epitope linked to the amino end of **HBcAg** is prepd. by expressing the corresponding chimeric gene in animal cells. The DNA encoding amino acid residues 142-160 of VP1 (VP1142-160) of 0-1-type foot-and-mouth disease virus (FMDV) isolated from plasmid pWRL 3123 was fused to the 5'-end of the DNA encoding **HBcAg** (from pWRL 201), sepd. by DNA encoding 6 amino acids of pre-**HBcAg**. The fused DNA was then used to construct plasmid pvFOHc based on a recombinant **vaccinia** virus shuttle vector pVp11k. CV-1 cells infected with pvFOHc produced the fusion protein contg. FMDV VP1142-160, which was detected by ELISA with antiserum to FMDV VP1141-160, FMDV virion, and to hepatitis B virus.

L2 ANSWER 28 OF 28 MEDLINE DUPLICATE 12
AN 84051483 MEDLINE
DN 84051483 PubMed ID: 6357119
TI Falciparum **malaria** and beta-thalassaemia trait in northern Liberia.
AU Willcox M; Bjorkman A; Brohult J
SO ANNALS OF TROPICAL MEDICINE AND PARASITOLOGY, (1983 Aug) 77 (4) 335-47.
Journal code: 2985178R. ISSN: 0003-4983.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198312
ED Entered STN: 19900319
Last Updated on STN: 19900319
Entered Medline: 19831220
AB In a study in northern Liberia of the **malaria** and beta-thalassaemia hypothesis, the frequencies of beta-thalassaemia and HbS traits were 9.1 and 3.4% in the Mano and 9.5 and 1.7% in the Gio tribal samples. **HbC** and HbN were present at low frequency. G6PD

deficiency was found in 16% of males. An observed increase with age of beta-thalassaemia trait frequencies was consistent with the selection hypothesis. However, we could not entirely exclude that associated iron deficiency influenced the results in the six to 11 month age group. **Malaria** was holoendemic; **Plasmodium** falciparum predominated, P. malariae and P. ovale were also identified. **Plasmodium** falciparum prevalence rates were similar in normal and beta-thalassaemia trait children but parasite densities were consistently lower in the latter. Using the criterion of a falciparum parasite density of 1 x 10(9) 1(-1) or greater to indicate a potentially important infection, the relative risk in beta-thalassaemia traits one to four years old from the cross-sectional study was 0.45 (upper 95% confidence interval 0.79) and 0.41 (0.61) in two to nine year trait carriers from a longitudinal study. **Plasmodium** falciparum gametocyte rates were lower in beta-thalassaemia trait children (P less than 0.005). The geometric mean titre of P. falciparum antibodies was lower in beta-thalassaemia trait children from the one to four year group (P less than 0.05). Otherwise **immunological** studies showed little difference between the different Hb types. Parasitological findings were consistent with relative resistance of HbS trait carriers towards P. falciparum infection. We found no evidence for relative resistance of beta-thalassaemia traits towards P. malariae infection nor that G6PD deficient males were more resistant to P. falciparum than those with normal activity. We conclude that the results are consistent with relative resistance of beta-thalassaemia trait carriers to P. falciparum **malaria**.